

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising the DNA sequence set forth in Figure 1 (SEQ ID NO:1) or degenerate variants thereof.
2. An isolated nucleic acid molecule or degenerate variants thereof, hybridizable to said DNA sequence of Claim 1 under standard hybridization conditions.
3. The isolated nucleic acid molecule of Claim 1 or 2, which encodes a polypeptide having an amino acid sequence as set forth in Figure 2 (SEQ ID NO:2), or conserved variants thereof.
4. An isolated nucleic acid molecule comprising the DNA sequence set forth in SEQ ID NO:3, or degenerate variants thereof.
5. An isolated nucleic acid molecule or degenerate variants thereof, hybridizable to said cDNA sequence of Claim 3 under standard hybridization conditions.
6. The isolated nucleic acid molecule of Claim 4 or 5, which encodes a polypeptide having an amino acid sequence as set forth in Figure 4 (SEQ ID NO:4), or conserved variants thereof.
7. A detectably labeled nucleic acid hybridizable to an isolated nucleic acid molecule as set forth in Claim 1, 2, 4 or 5.
8. The detectably labeled nucleic acid of Claim 7, wherein said detectable label comprises radioactive isotopes incorporated into the structure of said nucleic acid.

9. A polypeptide having an amino acid sequence as set forth in Figure 2 (SEQ ID NO:2) or a fragment thereof. or Figure 4 (SEQ ID NO:4) or a fragment thereof.

5 10. An antibody having the polypeptide of Claim 7 as an immunogen.

11. The antibody of Claim 10, wherein said antibody is a monoclonal antibody.

10 12. The antibody of Claim 10, wherein said antibody is a polyclonal antibody.

13. The antibody of Claim 10, wherein said antibody is a chimeric antibody.

15 14. The antibody of any of Claims 10-13, wherein said antibody is detectably labeled.

15 15. The antibody of Claim 14, wherein a detectable label is selected from the group consisting of alkaline phosphatase, peroxidase, and radioactive isotopes
20 incorporated into the antibody.

16. An expression vector containing said isolated nucleic acid molecule of Claim 1 operatively associated with a promoter.

25 17. An expression vector containing said isolated nucleic acid molecule of Claim 2 operatively associated with a promoter.

18. An expression vector containing said isolated nucleic acid molecule of Claim 3 operatively associated with a promoter.

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19. An expression vector containing said isolated nucleic acid molecule of

Claim 4 operatively associated with a promoter.

20. An expression vector containing said isolated nucleic acid molecule of Claim 5 operatively associated with a promoter.

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21. The expression vector of any of Claims 16-20, wherein said promoter is selected from the group consisting of the immediate early promoters of hCMV, early promoters of SV40, early promoters of adenovirus, early promoters of vaccinia, early promoters of polyoma, late promoters of SV40, late promoters of adenovirus, late promoters of vaccinia, late promoters of polyoma, the *lac* the *trp* system, the *TAC* system, the *TRC* system, the major operator and promoter regions of phage lambda, control regions of fd coat protein, 3-phosphoglycerate kinase promoter, acid phosphatase promoter, promoters of yeast α mating factor.

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22. A unicellular host transformed with an expression vector of Claim 21.

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23. The unicellular host according to Claim 22, wherein said host cell is selected from the group consisting of *E. coli*, *Pseudomonas*, *Bacillus*, *Streptomyces*, yeast, CHO, R1.1, B-W, L-M, COS1, COS7, BSC1, BSC40, BMF10 and Sf9 cells.

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24. A mammalian cell containing a TRANCE encoding DNA sequence and modified *in vitro* to permit higher expression of TRANCE by means of a homologous recombinational event consisting of inserting a promoter in functional proximity to the TRANCE polypeptide encoding sequence.

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25. A cell according to Claim wherein the promoter is a TRANCE polypeptide promoter and the homologous recombinational event replaces a mutant TRANCE polypeptide promoter.

26. A cell according to Claim, wherein the promoter insert is not a TRANCE promoter.

27. A method of producing the polypeptide of Claim 7, comprising the steps of:

a) culturing a unicellular host according to Claim 22 under conditions that provide for expression of the polypeptide of Claim 7; and

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b) recovering the polypeptide from the cell and the culture.

28. A modulator of immune response in a mammal, wherein said modulator is selected from the group consisting of:

10 a) a polypeptide having an amino acid sequence set forth in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4) or degenerate variants thereof, or a fragment thereof;

b) an analog or derivative of a polypeptide having an amino acid as set forth in Figure 2 (SEQ ID NO:2), SEQ ID NO:4, or degenerate variants thereof, or a fragment thereof; fusion protein containing the amino acid sequence of Figure 2 (SEQ
15 ID NO:2) or a fragment thereof;

c) a fusion protein wherein its amino acid sequence contains an amino acid sequence of Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), degenerate variants thereof, or a fragment thereof;

d) an antibody having an immunogen selected from the group consisting of:

20 i) a polypeptide having an amino acid sequence set forth in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4) or degenerate variants thereof, or a fragment thereof;

ii) an analog or derivative of a polypeptide having an amino acid as set forth in Figure 2 (SEQ ID NO:2), SEQ ID NO:4, or degenerate variants thereof, or a
25 fragment thereof; fusion protein containing the amino acid sequence of Figure 2 (SEQ ID NO:2) or a fragment thereof;

iii) a fusion protein wherein its amino acid sequence contains an amino acid sequence of Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), degenerate variants thereof, or a fragment thereof;

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and

d) an anti-sense TRANCE nucleic acid comprising at least one phosphodiester

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analog bond.

29. An analog or derivative of TRANCE, wherein the chemical moiety is a water-soluble polymer.

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30. An analog or derivative of Claim 29, wherein the water soluble polymer is polyethylene glycol.

32. An analog or derivative of Claim 30 which is mono-, di-, tri- or
10 tetrapegylated.

33. An analog or derivative of Claim 31, which is N-terminal monopegylated.

34. The modulator of immune response in a mammal as set forth in Claim 28,
15 wherein said modulator is an agonist of TRANCE and modulates immune response by increasing the life span of mature dendritic cells, wherein said modulator is selected from the group consisting of:

- a) a polypeptide having an amino acid sequence set forth in Figure 2 (SEQ ID NO:2) . Figure 4 (SEQ ID NO:4) or degenerate variants thereof, or a fragment thereof;
- 20 b) an analog or derivative of a polypeptide having an amino acid as set forth in Figure 2 (SEQ ID NO:2), SEQ ID NO:4, or degenerate variants thereof, or a fragment thereof; fusion protein containing the amino acid sequence of Figure 2 (SEQ ID NO:2) or a fragment thereof; and
- c) a fusion protein wherein its amino acid sequence contains an amino acid
25 sequence of Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), degenerate variants thereof, or a fragment thereof.

35. The modulator of immune response in a mammal as set forth in Claim 28, wherein said modulator is an antagonist of TRANCE and modulates immune response
30 by decreasing the life span of mature dendritic cells, wherein said modulator is selected from the group consisting of:

an antibody having an immunogen selected from the group consisting of:

i) a polypeptide having an amino acid sequence set forth in Figure 2 (SEQ ID NO:2) . Figure 4 (SEQ ID NO:4) or degenerate variants thereof, or a fragment thereof;

5 ii) an analog or derivative of a polypeptide having an amino acid as set forth in Figure 2 (SEQ ID NO:2), SEQ ID NO:4, or degenerate variants thereof, or a fragment thereof; fusion protein containing the amino acid sequence of Figure 2 (SEQ ID NO:2) or a fragment thereof; and

10 iii) a fusion protein wherein its amino acid sequence contains an amino acid sequence of Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), degenerate variants thereof, or a fragment thereof;

and

b) the anti-sense TRANCE nucleic acid comprising at least one phosphodiester analog bond.

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36. The modulator of immune response in a mammal as set forth in Claim 28, wherein said modulator is an agonist of TRANCE and modulates immune response by increasing T cell activation in a mammal, and said modulator is selected from the group consisting of:

20 a) a polypeptide having an amino acid sequence set forth in Figure 2 (SEQ ID NO:2) , Figure 4 (SEQ ID NO:4) or degenerate variants thereof, or a fragment thereof;

b) an analog or derivative of a polypeptide having an amino acid as set forth in Figure 2 (SEQ ID NO:2), SEQ ID NO:4, or degenerate variants thereof, or a fragment thereof; fusion protein containing the amino acid sequence of Figure 2 (SEQ ID NO:2) or a fragment thereof; and

25 c) a fusion protein wherein its amino acid sequence contains an amino acid sequence of Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), degenerate variants thereof, or a fragment thereof.

30 37. The modulator of immune response in a mammal as set forth in Claim 28, wherein said modulator is an antagonist of TRANCE modulates immune response by

decreasing T cell activation in a mammal, and said modulator is selected from the group consisting of:

an antibody having an immunogen selected from the group consisting of:

5 i) a polypeptide having an amino acid sequence set forth in Figure 2 (SEQ ID NO:2) , Figure 4 (SEQ ID NO:4) or degenerate variants thereof, or a fragment thereof;

ii) an analog or derivative of a polypeptide having an amino acid as set forth in Figure 2 (SEQ ID NO:2), SEQ ID NO:4, or degenerate variants thereof, or a fragment thereof; fusion protein containing amino acid sequence of Figure 2 (SEQ ID NO:2) or a fragment thereof; and

10 iii) a fusion protein wherein its amino acid sequence contains an amino acid sequence of Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:4), degenerate variants thereof, or a fragment thereof;

15 and

b) the anti-sense TRANCE nucleic acid comprising at least one

38. A TRANCE agonist pharmaceutical composition comprising said modulator of Claim 36 and a pharmaceutically acceptable carrier thereof.

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39. A method for treating an immune system related condition in a mammal, said method comprising the steps of:

a) exposing at least one mature dendritic cell of the mammal to an antigen so that the at least one mature dendritic cell can present the antigen on its surface; and

25 b) administering to the mammal a therapeutically effective amount of a TRANCE agonist pharmaceutical composition of Claim 38.

40. The method for treating an immune system related condition as set forth in Claim 39, wherein said antigen is selected from the group consisting of:

30 a) a pathogen. or a fragment thereof;

- b) a virus, or a fragment thereof; and
- d) a tumor, or a fragment thereof.

41. The method for treating an immune system related condition as set forth
5 in Claim 40, wherein the immune system related condition is HIV or cancer.

42. The method for treating an immune system related condition as set forth
in Claim 40, wherein said pharmaceutically composition is administered orally,
pulmonarily, or nasally.

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43. The method for treating an immune system related condition as set forth
in Claim 39, further comprising the steps of removing the at least one mature dendritic
cell from the mammal prior to the exposing step, and reintroducing the mature
dendritic cell into the mammal after the exposing step, and prior to the administering
15 step.

44. The method for treating an immune system related condition as set forth
in Claim 43, wherein the antigen is selected from the group consisting of:

- a) a pathogen, or a fragment thereof:
- 20 b) a virus, or a fragment thereof; and
- c) a tumor, or a fragment thereof.

45. The method for treating an immune system related condition as set forth
in Claim 44, wherein the immune system related condition is HIV or cancer.

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46. The method for treating an immune system related condition as set forth
in Claim 45, wherein said pharmaceutical composition is administered orally,
pulmonarily, or nasally.

30 47. A TRANCE antagonist pharmaceutical composition comprising said
modulator of Claim 35 and a pharmaceutically acceptable carrier thereof.

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48. A method for treating an immune system related condition in a mammal, comprising administering to the mammal a therapeutically effective amount of the TRANCE antagonist pharmaceutical composition of Claim 47.

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49. The method for treating an immune system related condition in a mammal as set forth in Claim 48, wherein said condition is related to over-expression of TRANCE protein in the mammal.

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50. The method for treating an immune system related condition in a mammal as set forth in Claim 49, wherein said condition is an autoimmune disease or hypersensitivity to an allergen.

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51. A method for modulating levels of expression of a TRANCE protein in a mammal, comprising the steps of:

a) removing at least one hematopoietic stem cell from the mammal;

b) destroying remaining hematopoietic stem cells in the mammal;

c) transfecting the at least one hematopoietic stem cell with a vector containing a nucleic acid molecule which encodes a TRANCE protein such that the nucleic acid molecule becomes incorporated into the genome of the hematopoietic stem cell, forming a transfected hematopoietic stem cell; and

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d) introducing the transfected hematopoietic stem into the mammal so that the transfected hematopoietic stem cell can self replicate and differentiate within the mammal.

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52. The method for modifying levels of expression of a TRANCE protein in a mammal as set forth in Claim 51, wherein the nucleic acid molecule has a DNA sequence as set forth in Figure 1 (SEQ ID NO:1) or degenerate variants thereof.

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53. A method of diagnosing an immune system related condition in a mammal, wherein the method comprises the steps of:

- a) removing a bodily sample from the mammal;
- b) assaying the bodily sample to determine whether TRANCE is expressed in the bodily sample.

5 54. The method of diagnosing an immune system related condition in a mammal as set forth in Claim 53, wherein the mammal is a human.

 55. The method of diagnosing an immune system related condition as set forth in Claim 54, wherein the TRANCE protein is encoded by a nucleic acid
10 molecule having a DNA sequence as set forth in Figure 1 (SEQ ID NO:1), or degenerate variants thereof.

 56. The method of diagnosing an immune system related condition as set forth in Claim 55, wherein TRANCE has an amino acid sequence as set forth in
15 Figure 2 (SEQ ID NO:2), or conserved variants thereof.

 57. The method of diagnosing an immune system related condition of Claim 56, wherein the bodily sample is blood or lymphoid tissue.

20 58. The method of diagnosing an immune system related condition of Claim 57, wherein said lymphoid tissue is selected from the group consisting of lymph node tissue, spleen tissue, and thymus tissue.

 59. The method of diagnosing an immune system related condition of Claim
25 58, wherein the immune system related condition is an autoimmune disease.

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